

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims

1-36 Cancel.

37. (new) A protein array comprising a surface having a plurality of spatially defined locations wherein at each location there are deposited at least two protein moieties which are capable of forming a complex characterized in that said complex is transiently formed.

38. (new) The protein array of claim 37 wherein the complex is transiently formed during catalysis.

39. (new) A protein array comprising a surface having a plurality of spatially defined locations wherein at each location there are deposited at least two protein moieties characterized in that said protein moieties at each location act sequentially on a substrate of interest.

40. (new) The protein array of claim 37 wherein at least one of said protein moieties at each location is capable of being membrane-associated or membrane-bound or has been modified to interact with a non-polar or amphipathic molecule.

41. (new) The protein array of claim 37 wherein at least one of said moieties at each location is a drug metabolizing enzyme.

42. (new) A protein array comprising a surface upon which are deposited at spatially defined locations at least two protein moieties characterized in that said protein moieties are derived from one or more drug metabolizing enzymes.

43. (new) The protein array of claim 41 wherein at least one of said protein moieties at each location is a P450 protein.
44. (new) The protein array of claim 39 wherein said protein moieties are attached to said surface through a marker moiety appended to each protein moiety.
45. (new) The protein array of claim 37 wherein said protein moieties are incorporated into a membrane, vesicle or liposome which is immobilised in proximity to said surface.
46. (new) The protein array of claim 41 wherein said drug metabolizing enzymes are selected from the group consisting of cytochrome P450s, flavin monooxygenases, UDP glycosyltransferases, glutathione S-transferases, sulfotransferases and N-acetyltransferases.
47. (new) The protein array of claim 39 said array comprises one or more Phase 1 drug metabolizing enzymes and one or more Phase 2 drug metabolizing enzymes.
48. (new) The protein array of claim 41 wherein said drug metabolizing enzymes are H. sapiens cytochrome P450s and are selected from the group consisting of COPIA2, CYP2A6, CYP2B6, CYP2C8, CYP2C9*1, CYP2C9*2, CYP2C9*3, CYP2C19, CYP2D6, CYP2E1, CYP3A4 and CYP3A5.
49. (new) The protein array of claim 41 wherein one or more of said drug metabolizing enzymes are derived from different ethnic groups, different genders, different mammalian species, or different mutant versions of a wild type enzyme.
50. (new) A method of making a protein array comprising the steps of :
- a) providing two or more drug metabolizing enzymes of interest from a recombinant source, a native source or a synthetic source; and
 - b) depositing said proteins at spatially defined locations on a surface to make said protein array.

51. (new) The method of claim 50, wherein said drug metabolizing enzymes are brought into contact with the array in admixture with other protein molecules and deposition on the array occurs with simultaneous purification of the protein moiety on the array via a tag incorporated in the protein moiety.
52. (new) The method of claim 50, wherein said drug metabolizing enzymes are deposited with other proteins from an expression host cell on a surface at spatially defined locations to make said protein array.
53. (new) An array made by the method of claim 50.
54. (new) A method of making a protein array comprising the steps of :
- a) providing one or more proteins from either recombinant, native or synthetic sources incorporated in purified or partially purified membrane or membrane-like preparations; and
 - b) arraying said proteins by encapsulation of said membrane or membrane-like preparations into a gel matrix which is deposited on the surface.
55. (new) A method of making an array of drug metabolizing enzymes comprising the steps of :
- a) providing drug metabolizing enzymes from either recombinant, native or synthetic sources in the form of purified or partially purified membrane or membrane-like preparations; and
 - b) arraying said drug metabolizing enzymes either by deposition of said membrane or membrane-like preparations onto a suitable surface capable of capturing the membranes or by encapsulation of said membrane or membrane-like preparations into a gel matrix which is deposited on the surface.
56. (new) The method of claim 55 wherein one or more of said membrane or membrane-like preparations contains two or more different proteins.

57. (new) The method of claim 56 wherein said two or more different proteins are capable of forming a complex with each other.
58. (new) The method of claim 57 wherein said complex is transiently formed.
59. (new) The method of claim 56 wherein said two or more different proteins act sequentially on a substrate of interest.
60. (new) A method of screening a set of protein moieties for molecules which interact with one or more proteins comprising the steps of:
- a) bringing one or more test molecules into contact with an array as claimed in claim 37 which carries said set of protein moieties; and
 - b) detecting an interaction between one or more test molecules and one or more proteins on the array.
61. (new) A method of simultaneously determining the relative properties of members of a set of protein moieties, comprising the steps of:
- a) bringing an array as claimed in claim 37 which carries said set of protein moieties into contact with one or more test substances, and
 - b) observing the interaction of said test substances with the set members on the array.
62. (new) The method of claim 61 wherein one or more of said protein moieties are drug metabolizing enzymes and wherein said enzymes are activated by contact with an accessory protein or by chemical treatment.
63. (new) A method for determining a gender differences in drug metabolism comprising the steps of:
- a) providing a male drug metabolizing enzyme array of claim 41;
 - b) providing a female drug metabolizing enzyme array of claim 41;

- c) bringing said arrays into contact with one or more test substances; and
- d) observing a difference in the interaction of said test substances with the drug metabolizing enzymes of the two array.

64. (new) A method for determining an ethnic difference in drug metabolism comprising the steps of:

- a) providing drug metabolizing enzyme array of claim 41 from a first ethnic group;
- b) providing drug metabolizing enzyme array of claim 41 from a second ethnic group;
- c) bringing said arrays into contact with one or more test substances; and
- d) observing a difference in the interaction of said test substances with the drug metabolizing enzymes of the two array.

65 (new) A method for determining a difference in drug metabolism in two mammalian species comprising the steps of:

- a) providing drug metabolizing enzyme array of claim 41 from a first mammalian species;
- b) providing drug metabolizing enzyme array of claim 41 from a second mammalian species;
- c) bringing said arrays into contact with one or more test substances; and
- d) observing a difference in the interaction of said test substances with the drug metabolizing enzymes of the two array.

66. (new) The method of claim 29 wherein said mammalian species are human and rat.

67. (new) A method for determining the cytotoxicity of drug metabolites comprising the steps of:

- a) providing drug metabolizing enzyme array of claim 41;
- b) overlaying said array with cells that act as reporters in a cytotoxicity assay;
- c) bringing said arrays into contact with one or more test substances; and

- d) observing an interaction between any metabolites produced by the drug metabolizing enzyme and said cells.
68. (new) A method for determining and quantitating of metabolic pathways for small molecules comprising the steps of:
- a) providing drug metabolizing enzyme array of claim 41;
 - b) bringing said arrays into contact with one or more small molecules; and
 - c) observing in interaction between said one or more small molecules and said drug metabolizing enzyme array to determine and quantitate said metabolic pathway.
69. (new) A method for screening compounds for their ability to bind and inhibit individual drug metabolizing enzymes comprising the steps of:
- a) providing drug metabolizing enzyme array of claim 41;
 - b) bringing said arrays into contact with one or more compounds; and
 - c) observing the binding or inhibition of said compounds with said drug metabolizing enzyme array.
70. (new) A method for determining the induction of P450 expression by one or more drugs comprising the steps of:
- a) providing a p450 array of claim 46 from a normal tissue;
 - b) providing a P450 array of claim 46 from a tissue treated with said one or more drugs; and
 - c) observing a difference in the distribution of said P450 array to determine an induction of P450 expression by said one or more drugs.
71. (new) A method for analyzing the effects of mutation on the activity of a drug metabolizing enzyme of interest comprising the steps of:
- a) providing a first drug metabolizing enzyme array of claim 41 wherein said drug metabolizing enzyme is mutated;
 - b) providing a second drug metabolizing enzyme array of claim 41;
 - c) bringing said arrays into contact with one or more compounds; and

- d) observing a difference in interaction between said one or more compounds and said arrays.

72. (new) A method of expressing and purifying a drug metabolizing enzyme, comprising the steps of:

- a) expressing a drug metabolizing enzyme of interest in a host cell;
- b) subjecting said host cell to conditions suitable to lyse the cell;
- c) obtaining a membrane associated cell fraction from the lysed cell;
- d) solubilizing said membrane associated cell fraction by the addition of a detergent;
- e) after an incubation period sufficient to solubilize the drug metabolizing enzyme protein contained in said membrane associated cell fraction, performing a further centrifugation step to produce a supernatant containing said drug metabolizing enzyme protein; and
- f) subjecting said supernatant to chromatography to purify said drug metabolizing enzyme protein.